REMARKS

Applicants express their appreciation to Examiners Wilson and McIntosh III for conducting telephone interviews with Applicants in August of 2004. During the interviews, Applicants discussed with the Examiners the patentability issue under 35 U.S.C. §103(a) raised in the Office Action mailed June 29, 2004. Claims 17, 22-24 and 26-53 have been cancelled. Claims 1-16 and 18-20 has been amended. Claims 1-16, 18-21 and 25 are now pending.

Claims 1-16, 18-21, 23 and 25 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Rubinfeld (US Patent No: 6,191,119) in view of Achterrath (US Patent No: 6,403,569).

Independent claim 1 as amended specifies a method for treating cancer in a cancer patient with p53 mutation by using a sequential therapy of a water-insoluble 20(S) camptothecin, 9-nitro-20(S)-camptothecin (9NC) or 9-amino-20(S)-camptothecin (9AC), and 5-fluorouracil (5-FU). Support for the claim language appears in the Specification, for example, at page 7, lines 7-15.

As discussed during the interviews, the claimed method is used for treating cancer in a patient with mutation in the tumor suppressor gene p53. According to the method, 9NC or 9AC is administered to the patient at least 1 day before or after administration of 5FU. None of the cited references teaches or suggests administering 9NC (or 9AC) at least 1 day before or after administration of 5FU in patient with p53 mutation. In fact, Applicants' global search for the key word "p53" or "tumor suppressor" in these two cited patents yielded no hit.

As also discussed during the interviews, Rubinfeld neither teaches administering 9NC or 9AC to a cancer patient at least 1 day before or after administration of 5-FU, nor suggests that such a water insoluble campthecin compound should be administered while 5-FU is not present in a pharmaceutically active form in the body. Even if Rubinfeld suggests that 9NC may be combined with 5-FU to exert therapeutically synergistic effects on a patient, one of ordinary skill in the art would be motivated to administer these two drugs more or less concomitantly in order

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to maximize the synergistic effects, instead of waiting until 5-FU is no longer in a pharmaceutically active form in the body.

On the other hand, Achterrath merely teaches a combination therapy of a water soluble 5-camptothecin derivative CPT-11, fluorouracil (5-FU), and folinic acid (FA). The combination of CPT-11 and 5-FU is administered within a 24-hr time period. Column 5, lines 23-28. Thus, Achterrath fails to teach the claimed sequential therapy which involves administering a water insoluble camptothecin compound such as 9NC or 9AC at least 1 day before or after the administration of 5-FU.

In view of the failure of the cited references to teach or suggest the claimed sequential therapy for a cancer patient with p53 mutation, Applicants submit that a prima facie case of obviousness has not been established under 35 U.S.C. §103(a). Withdrawal of this ground of rejection is therefore respectfully requested.

CONCLUSION

Applicants believe that they are entitled to a letters patent, and respectfully solicit the Examiner to expedite prosecution of this patent to issuance. Should the Examiner have any questions, Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

Date: September 1, 2004 By: 

Shirley Chen, Ph.D.
Reg. No. 44,608

WILSON SONSINI GOODRICH & ROSATI
650 Page Mill Road
Palo Alto, CA 94304-1505
Direct dial: (650) 565-3856
Customer No. 021971